PNEUMONIA AT A BASE HOSPITAL

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Early in February, a commission was sent by Surgeon-General Gorgas to Texas to study the pneumonia existing there. This commission was composed of Rufus Cole, W. G. MacCallum and Oswald T. Avery, Contract Surgeons, U. S. Army, Captains A. R. Dochez and R. A. Kinsella, and Lieutenants F. G. Blake, T. M. Rivers, H. John, F. A. Stevens and Wm. C. Von Glahn, Medical Reserve Corps. This special study was undertaken at the base hospital, Fort Sam Houston, San Antonio, Texas. This hospital was chosen for this work merely because pneumonia was prevailing there to a large extent at the time, and also because of its proximity to the laboratory of the Southern Department, where facilities were available for carrying out the bacteriologic and pathologic examinations. It was thought that any facts disclosed by the study there might be applicable to other camps and base hospitals. Any general application of our observations, however, must be made with reservations, for it is possible that the conditions in other hospitals may be different from those found here, and therefore that the pneumonia existing in other hospitals may differ in essential details from that present in this one.

Our preliminary survey of the cases in the hospital made it evident that not all the cases were of the same variety and that our present knowledge did not permit a ready differentiation of the cases of the different kinds. An extensive statistical study was therefore out of the question, and we decided to make a very

careful clinical, bacteriologic and pathologic study of a limited number of cases.

The study was commenced, Feb. 1, 1918, and continued about six weeks. This paper is composed of extracts from the preliminary reports made by us to the Surgeon-General.

PART I. ETIOLOGY AND CLINICAL FEATURES OF THE PNEUMONIA OCCURRING IN THE HOSPITAL

TOGETHER WITH NOTES CONCERNING THE PLACE AND MODE OF INFECTION IN THE CASE OF POSTMEASLES BRONCHOPNEUMONIA[1]

By Rufus Cole, M.D.

Varieties of Pneumonia

The account of the results of our observations will be rendered more intelligible if we state briefly that we have found two distinct varieties of pneumonia in the wards of this hospital. First, there are present cases of acute lobar pneumonia, which are essentially identical with cases of this disease occurring in civil life. With all these cases pneumococci have been associated; second, there are present a large number of cases of bronchopneumonia, which differ essentially from the cases of the former disease in clinical features, pathology and etiology. The majority of these cases occur as complications or sequelae of measles, though they may undoubtedly follow other infectious diseases. The pathology of these cases is carefully described by Dr. MacCallum in his report. The etiologic agent in all the cases studied here has appeared to be a streptococcus producing lysis of red blood corpuscles when grown on a medium containing blood. Similar observations have also been made in other Army hospitals, and it seems probable that these streptococci are responsible for most of the bronchopneumonia occurring in the present epidemic of measles. Previous observations, however, suggest that other bacteria may also be responsible for cases with similar clinical and pathologic features. In the further dis-

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1. This part of the work was carried out with the assistance of Oswald T. Avery, A. R. Dochez, R. A. Kinsella, F. G. Blake, T. M. Rivers, H. John, and F. A. Stevens.

cussion, we shall refer to these two varieties of pneumonia as "acute lobar pneumonia" and "bronchopneumonia." Finally, there occurs, in no inconsiderable number of patients, a combination of these two types of disease, or infection with both pneumococci and streptococci. In these cases, one or the other of the two varieties of disease is probably primary, secondary infection later occurring with the subsequent development of the other variety.

Since the regular hospital data were not considered sufficient for our purposes, complete histories were obtained from a series of cases of both varieties, and our own physical examinations were made and the results carefully recorded. Thirty cases of bronchopneumonia, thirty-two cases of acute lobar pneumonia, and nine cases in which the two varieties of infection were present have been studied.

It was impossible to study all of the cases of pneumonia in the hospital in this way. Consequently, in a considerable number of cases coming to necropsy, the clinical data are slight. On the other hand, many of the cases studied by us ended in recovery, and consequently the pathologic lesions present can only be inferred from the knowledge obtained in the other cases in which necropsy was performed. In twelve cases of bronchopneumonia, however, the clinical observations could be correlated with the pathologic findings.

BRONCHOPNEUMONIA

Bacteriology. — The evidence that *Streptococcus haemolyticus* is the etiologic agent in these cases is given by the study of cultures made from the blood during life and from the organs and tissues of the body after death, and by the study of the sputum coughed directly from the lung.

Cultures from the blood during life were made in fifteen cases. In only two cases was a growth obtained. In these cases a pure growth of *S. haemolyticus* occurred. The cultures were made only within twenty-four hours of death, however. Studies of the bacteria present in specimens of sputum expectorated from the lung were made in all the cases. The method employed was practically that described previously for the study of the sputum in lobar pneumonia.

Specimens of sputum directly coughed from the lung were obtained in sterile containers. After the washing of portions of this sputum, cultures were made on the surface of blood agar plates, and a small portion of sputum was injected into a mouse. After the death of the mouse, the peritoneal exudate was examined microscopically, and cultures were made from this exudate and from the heart's blood.

In all the cases that we have classified as bronchopneumonia, the cultures from the sputum on blood agar plates showed the presence of *S. haemolyticus* in large numbers. In most of the cases in which the mouse test was carried out, examination of the heart's blood showed the presence of this organism (in sixteen out of seventeen cases). In thirteen of the specimens of sputum, *Bacillus influenzae* as well as *S. haemolyticus* was found on the plates. In five instances, the patients died and came to necropsy, and in these instances *B. influenzae* was also present in the affected lung. In eight instances, *B. influenzae* was also present in the heart's blood of the mouse. Whether this organism plays any part in this disease is not known. Its very frequent presence is of much interest.

Cultures were made from the infected areas in the lungs, the heart's blood, the pleura, the pericardium, and frequently from other organs of the patients coming to necropsy. In making cultures from the lungs, the pleura over the infected area was seared with a hot knife, and a cone-shaped piece of the lung was remove with sterile instruments. Cultures and smears were then made from the tip of the portion removed. In all of the cases diagnosed as bronchopneumonia during life and all of those cases coming to necropsy which showed the presence of the lesions described by Dr. MacCallum as interstitial bronchopneumonia, *S. haemolyticus* was found to be present in the affected portion of the lung, usually in pure culture. In most of the cases in which empyema occurred, these organisms were present in the fluid in pure cultures.

It was also the rule to find these organisms in the heart's blood after death. In a few cases influenza bacilli were also present in the blood and tissues, along with *S. haemolyticus*. These cases, however, did not differ from those in which the streptococcus was present alone.

Clinical Course.—The picture of the clinical course of the disease which can be constructed from our data is necessarily incomplete and possibly incorrect in certain details. It is hoped, however, that it may be amplified and corrected by more complete studies in other camps. The study of these cases has not made it possible to differentiate, clinically, between the cases showing the lesions described by Dr. MacCallum as interstitial bronchopneumonia, and those showing the lesions described by him as lobular pneumonia. Consequently, in our discussion all these cases are termed "bronchopneumonia."

Onset.—All the cases of this group have followed measles. In seven of our thirty cases, a history was obtained of a chronic cough, coryza or sore throat previous to the appearance of the symptoms of measles. Whether pneumonia is more likely to occur in those men who have had previous infections of the respiratory tract is not certain, but it is possible that this factor is of some, but not paramount, importance.

A considerable number of cases of measles show laryngeal infection, as shown by the occurrence of hoarseness and huskiness of the voice. That this is a true inflammatory lesion is shown by the fact that minute ulcerations may be present on the vocal cords.

The first definite symptoms of the disease are usually cough, fever, slight respiratory distress, and the expectoration of a mucopurulent sputum. All of these symptoms, as is known, usually occur in some degree during the febrile stage of measles. In certain cases of measles, the temperature does not fall with, or shortly after, the appearance of the rash, as is usually the case, but the fever continues and becomes higher and the symptoms mentioned increase in severity. In other cases the temperature falls to normal, and then after a period of from a few days to three weeks the temperature again becomes elevated and the symptoms mentioned become severe and characteristic of the disease. In none of the cases we have seen, however, nor in any of those of which we have histories, has there been a complete disappearance of all the symptoms referable to the respiratory tract during the interval between recovery from measles and onset of bronchopneumonia. Even in the cases in which the onset has occurred following the discharge of the patient from the hospital, it is quite certain that

cough or respiratory difficulty was present at the time of discharge and persisted up to the time of onset of the pneumonia.

In all the cases that we have observed, the onset has been gradual. In no case was there a chill with sudden elevation of temperature. Vomiting during the early period has been rare.

These observations, as well as the pathologic studies, indicate that the infection, as well as the lesion, is probably a descending one, and that no sharp line can be drawn either in time or symptoms, between the occurrence of the pharyngitis, laryngitis, bronchitis, and finally the bronchiolitis and bronchopneumonia.

Symptoms.—When the disease is well developed, the following are the common symptoms:

Fever: Usually the fever is not high, rarely going higher than 104 F., and even in the uncomplicated cases the temperature is frequently irregular. Wide diurnal sweeps of the temperature curve, however, have usually been associated with the presence of empyema.

Pulse: The pulse has not been extremely rapid, even in the cases near death. Special attention has not been given to the occurrence of irregularities.

Respiratory Distress: This is the most marked and characteristic symptom of the disease, and is usually present even in the early stages. This is quite distinct from the respiratory difficulty seen in acute lobar pneumonia, with the expiratory grunt. In bronchopneumonia the great difficulty is with inspiration, the accessory muscle then being strongly brought into action. Frequently the expansion of the chest wall is slight, but the diaphragmatic pull is powerful, the costal margin being drawn on, and the intracostal spaces being markedly retracted with each inspiration. The patients seem consciously to have difficulty in getting sufficient air into the chest, but the inspiratory phase is not prolonged. The respiratory rate is usually not extremely rapid; frequently, even in very ill patients, the rate is not over thirty per minute.

Cyanosis: This is practically always present, even in the early stages, and in the more severe cases becomes extreme.

Cough: The cough is troublesome; frequently it is markedly increased by change in posture.

Sputum: Usually the expectoration is fairly free and moderate in amount. Its character varies markedly in the different cases and in the different stages of the disease. Early in our studies it was thought that the sputum had a specific appearance, being light-greenish, mucopurulent, sometimes somewhat blood streaked, and of a homogeneous character, spreading like molasses over the bottom of a cup. Later,

however, typical cases have been observed in which this kind of sputum was never seen. In some cases the sputum has been nummular, quite mucoid, the masses being tenacious and somewhat sticky. In other cases the nummular masses have been greenish and very purulent. In none of the uncomplicated cases has the sputum been sticky and of a rusty color like that seen in acute lobar pneumonia, nor has it contained large amounts of bright-red blood, as is sometimes seen in the early stages of lobar pneumonia. Whatever its character, it practically always contains large numbers of pus cells.

Restlessness: This is a striking feature of the condition. The patients are fairly alert, rarely delirious, but always anxious and frequently frightened. Sleeplessness, probably due largely to the cough and respiratory difficulty, is very frequently present.

Pain: This is frequently one of the symptoms, and is due to the pleurisy which is almost invariably present. Abdominal pain, in the uncomplicated cases, has not been frequent in this series.

In the typical cases, the symptoms we have mentioned are quite striking and more or less characteristic. It must be remembered, however, that similar symptoms, though of milder grade, are also present in cases of bronchitis without involvement of the smaller bronchioles. The symptoms are characteristic enough in the severe cases, however, to differentiate them from cases of acute lobar pneumonia.

Signs.—We have already spoken of the obvious signs of respiratory distress and the cyanosis which is so striking. Physical examination of the chest may or may not reveal signs indicating consolidation. This, of course, depends on the intensity and focal distribution of the lesions. Where the process is very diffuse, the chest may be resonant throughout, on percussion, though in certain regions, especially at the bases, the percussion note is frequently impaired. On auscultation, râles are usually heard throughout the chest. There are frequently musical and squeaking, in addition to moist, crackling, râles. In typical cases, the râles are more numerous during inspiration, and the inspiratory murmur is harsh. In such cases, the expiratory murmur may be scarcely audible; even though the expiratory murmur is inaudible, however, a succession of medium, moist râles may be heard during the expiratory phase. Over the areas of impaired resonance the breath sounds may be very

faint or absent until after the patient coughs, when harsh, mucous râles are heard, and the breath sounds become audible.

In some cases characteristic signs of consolidation, impaired resonance, tubular breathing and intensified spoken and whispered voice sounds are present over small areas. Frequently these signs persist for a few days, and then entirely disappear. In our early cases, these signs were most confusing and difficult to interpret. As we became better acquainted with the pathologic lesions, however, the meaning became obvious. I shall not attempt to bring the signs into relation with the lesions, since this relation becomes quite clear on the reading of Dr. MacCallum's report.

In no uncomplicated cases have we seen wide areas of dulness with characteristic tubular breathing and other signs of consolidation. When these signs have been present, there was always a complicating lobar pneumonia. In a few cases, however, later in the disease, there has been impairment of the percussion note over a wide area, with quite distant tubular breathing over this area, but with voice sounds fairly well transmitted. The repeated insertion of a needle in these cases has failed to reveal fluid, and the needle has felt as though it were in a more or less solid lung. We have interpreted these signs as due to a quite widespread involvement of the lung, with a marked degree of proliferation and plugging of the bronchi, as described by Dr. MacCallum. These are probably the cases which go on to necrosis and abscess formation, such as was seen in three of the necropsy cases. It must be remembered, however, that in the only cases of this type that we have seen at necropsy there was a marked accumulation of fluid in the pleura.

Complications.—Focal infections, such as tonsillitis and otitis media, may be present. They have not occurred frequently in this series, however. The most important complication is empyema.

Empyema.—This condition occurs with great frequency, being present in sixteen of the thirty cases, and in all but one of the necropsy cases. In ten of the cases, the condition was diagnosed by aspiration of fluid from the chest during life. In four additional cases, fluid was obtained from the chest on aspiration, but in these cases, the fluid was only slightly turbid, and contained no bacteria demonstrable by culture.

The diagnosis of the presence of fluid or pus in the pleural cavity in these cases is frequently difficult. In the cases in which large accumulations of fluid have occurred, no great skill is required. It is probably of great importance, however, to detect the presence of small amounts of fluid, and to do this as early after the fluid appears as possible. Small amounts of fluid can be detected only by employing the methods of physical examination of the chest. Roentgen examination is of assistance in certain cases. We have already stated that occasionally, over the more intensely affected areas, there is dulness on percussion, and the breath sounds may be distant. To determine whether these signs are due to an intrapulmonary lesion or to the accumulation of fluid in the pleural cavity is frequently very difficult. The greater intensity of the dulness on percussion, when fluid is present, and the distant faint tubular breathing heard at the margin of the area, are the signs of greater importance. Fortunately, the decision can be obtained by insertion of a needle, and in doubtful cases, this may be done not only once, but many times, if necessary.

Character of the Fluid: In most of our cases, the fluid obtained has been thin, but turbid, owing to the presence of bacteria and numerous fibrinous, purulent floccules. In only three or four cases has a thick, greenish-yellow pus been encountered. The infrequency of an exudate of this character should lead one to suspect, when such fluid is found, that the condition is a complication of lobar pneumonia and not of bronchopneumonia.

Mortality.—Of the thirty patients studied by us, fourteen died and sixteen recovered, a mortality of 47 per cent. Several of the patients are still very ill, however, and will probably die. Since the cases were not taken in succession, it is impossible to say whether or not this is a fair estimate of the mortality rate. Probably the percentage of cases ending fatally in this hospital has been considerably higher than this. A most striking fact is that all the necropsy cases in our series were complicated by empyema. In many cases it has seemed that death was related directly to this complication.

Treatment.—No observations were made on the effect of any special form of treatment. Since the occurrence of empyema is an important factor in the

outcome of the treatment of this complication, it deserves a few words of discussion.

Seven of the empyema patients were operated on, a rib resection with drainage being performed in each case. Of these patients, four have died. All of the others are very sick, and a fatal outcome is probable in one or more. On the other hand, of four patients in whom fluid containing streptococci was aspirated from the chest and operation was not performed, all have died. There were three cases in which fluid containing a moderate number of pus cells but no bacteria was aspirated from the chest. One of these patients was operated on; the other two were not. All three of these patients have lived, and from present indications will probably recover, though the patient operated on is still very ill. Our observations are not sufficient to enable us to draw any conclusions as to operation in this condition. They suggest, however, that in the cases in which fluid containing streptococci is aspirated from the lung, the chest should be opened and drained. But the question of operation in these cases is a difficult one, and we cannot be guided entirely by our experience with empyema complicating lobar pneumonia. The problem deserves special study.

LOBAR PNEUMONIA

During the course of our study of cases of bronchopneumonia, a considerable number of cases of typical lobar pneumonia were encountered. Some of these were chosen for study deliberately in order to have a control for the other work; in some the differential diagnosis was made only after careful investigation. One purpose of this study was to demonstrate to the hospital and laboratory personnel the fact that, under the conditions existing here, rapid and accurate diagnosis of the type of pneumococcus causing the infection in lobar pneumonia could be made. A small number of the patients were treated with serum by us or under our direction. This was also done for the purpose of demonstration.

Thirty-two cases of lobar pneumonia were studied. Only two of these patients had recently had measles: one one month, and the other six weeks previous to onset. There seemed no definite relation between the measles and pneumonia in these cases. In one other

case, not included in this series, an apparent pulmonary infection with pneumococcus Type IV occurred during convalescence from measles. There was a pleural exudation of clear, sterile fluid; but the signs of lobar pneumonia were never definite.

Of these cases, seventeen were associated with Type I pneumococcus in the sputum; three with Type II; four with atypical Type II; one with Type III; six with Type IV, and one with *Streptococcus mucosus*.

The etiologic diagnosis was made within twenty-four hours in all these cases except two. In these cases, the delay was due to the fact that the sputum was very scanty and unsatisfactory, and the tests had to be repeated. The examination in both of these cases was made late in the disease. (Some of the patients were studied on admission, others only after they had been in the wards for some days.) In seventeen cases, the diagnosis was made within eight hours, the Avery medium being employed. Considering the conditions under which we worked, this result seems quite satisfactory and demonstrates the possibility of type determinations in a military hospital.

In eleven cases, the presence of fluid in the chest was determined by aspiration. In five cases the fluid was clear, or very slightly turbid. In four of these cases the fluid was sterile; in the remaining case the fluid was contaminated after renewal from the chest and cultures could not be made. In these five cases, the fluid was removed by aspiration, and all the patients recovered without operation. In five other cases, the fluid was very turbid, and cultures revealed the presence of pneumococcus Type I. All of these patients were drained. Three of them are now well or are satisfactorily convalescing. Two of them are still very ill and have irregular fever. In the remaining case the fluid was thick and green, and cultures showed the presence of pneumococcus Type II. This patient was operated on and is also convalescing.

In eight of the Type I cases, the patients were treated with serum. Two of the treated patients were found to be sensitive to horse serum, and it was necessary to desensitize them before the administration of large amounts of serum. All but one recovered promptly; this one developed empyema. This patient

has done well since operation and is now convalescent. The results of this small series of cases, therefore, were satisfactory.

Of the thirty-two patients, two died; two of the empyema patients are still ill, and the result is in doubt. The others have recovered.

This experience with lobar pneumonia in this hospital leads us to believe that it does not differ essentially from that seen in civil hospitals, except, perhaps, in its relative mildness. This, however, is to be expected in a population composed of healthy young adults.

CASES OF MIXED INFECTION OR DOUBTFUL CASES

In addition to the cases which were clinically identified as bronchopneumonia and which at necropsy were found to show the lesions described as interstitial bronchopneumonia or lobular pneumonia, and the cases which were typically lobar pneumonia, both clinically and at necropsy, there occurred a series of cases which were more or less complex in their clinical, etiologic and pathologic features.

There were seven cases in which evidence was obtained of a mixed infection with pneumococcus and *S. haemolyticus,* the infections being present simultaneously or in succession. Four of these cases were in patients who had recently had measles:

The first patient had signs of bronchopneumonia beginning a few days after measles. Four days later there was an acute exacerbation of symptoms with signs resembling pneumonia. This patient developed empyema on the side of the lobar involvement; and from this fluid during life pneumococcus Type IV was obtained. Death came six days after the onset of the severe symptom. The necropsy showed the presence of lobar pneumonia of the left lower lobe and an area of typical bronchopneumonia in other portions of the lung. From the blood and the right lung, *S. haemolyticus* was isolated. From the pleural exudate both *S. haemolyticus* and pneumococcus Type IV were cultivated. That a combined infection in this case was present is certain. The chronologic course of events is more difficult to decide. It is impossible to say definitely whether the patient had a bronchopneumonia, with secondary pneumococcus infection, which led to septicemia and death, or whether the streptococcus infection occurred later, or finally whether the two infections occurred simultaneously.

The second patient had otitis media and also pulmonary symptoms lasting almost a month following measles. There then occurred an exacerbation of signs and symptoms, and the ward surgeon made a diagnosis of pneumonia. We saw him two days later and found an empyema on the left side, in addition to some signs of consolidation of the left lower lobe. The fluid from the chest contained *S. haemolyticus*, but the blood culture showed the presence of pneumococcus Type IV. The patient died two days later, and at necropsy a true lobar pneumonia was present, but no evidences of bronchopneumonia. In the cultures at necropsy, only *S. haemolyticus* was obtained from both lungs, and *S. haemolyticus* and *B. influenzae* from the blood. This case is difficult to interpret. The patient had a lobar pneumonia, and this was probably due to pneumococcus Type IV, although for some unexplained reason these organisms were not found at necropsy. Whether the streptococcus infection occcurred early in the illness or only shortly before death cannot be determined. Unfortunately, the early clinical notes are incomplete, and we have no knowledge of the severity of the early lung involvement.

The third patient developed fever and respiratory symptoms ten days after an attack of measles. In the interval, however, he had had slight, irregular fever. We saw him four days later. He had then only signs of diffuse lung involvement, with indications of empyema on the left side. The sputum contained *S. haemolyticus*, as did also the purulent fluid aspirated from the chest. No pneumococci were isolated. Four days later he was operated on, and the pleural cavity was drained. He lived almost two weeks, and then died. At necropsy an undrained pocket of pus was found between the left lung and the pericardium, and in addition there was almost complete uniform consolidation of the entire left lung. The other lung showed no evidences of bronchopneumonia. At necropsy, *S. haemolyticus* was found in all the cultures, as well as a gram-negative bacillus producing a putrefactive odor. In this case lobar pneumonia existed without the presence of pneumococci being demonstrated at any time. This may have been due, however, to the overgrowth of the culture with a putrefactive organism, which was undoubtedly a terminal invader. When the lobar pneumonia began, or whether bronchopneumonia was ever present, cannot, of course, be decided.

The fourth patient developed typical lobar pneumonia during convalescence from measles. The blood culture showed the presence of pneumococcus Type I. He developed fluid in the left chest which was purulent, and contained pneumococcus Type I and *S. haemolyticus*. He died three days after the tapping, and at necropsy no pneumonia was found, but several small abscesses in the left lung and a very large

amount of purulent exudate in the left pleura. The necropsy culture showed only the presence of streptococci. No pneumococci grew.

There were three patients suffering from acute lobar pneumonia in the pneumonia wards who gave no history of measles but in whom evidence of additional infection with *S. haemolyticus* was obtained. In two of these cases the pneumococcus causing the lobar pneumonia was Type II; in one, Type I.

One of these patients, during convalescence from pneumonia due to pneumococcus Type II, developed empyema, and the pleural exudate contained *S. haemolyticus* and *B. influenzae.* He had had some cough and sore throat for three weeks before the onset of pneumonia, and it is possible that the streptococcus infection antedated the pneumonia. There is no definite evidence for this, however.

The second patient had quite a typical attack of acute lobar pneumonia, also due to pneumococcus Type II. He gave no history of any pulmonary symptoms previous to the onset of pneumonia. During convalescence, he developed an irregular fever and signs of scattered lesions in the chest. There occurred an effusion of fluid in the pleura, cultures from which were sterile. The examination of the sputum at this time, however, revealed the presence of *S. Haemolyticus,* which had previously been absent. In spite of the fact that the chest fluid was sterile, the chest was opened and drained. The signs of diffuse involvement of the lungs, however, continued, and the patient, one week after operation, is still seriously ill. The study of this case is incomplete, and the evidence of secondary streptococcus infection is not satisfactory, but is suggestive.

The third patient suffered from acute lobar pneumonia, due to pneumococcus Type I, involving the right lower lobe. Convalescence was normal for a week. Signs of pulmonary involvement persisted, however. At the end of the week, the temperature again became elevated, and the presence of fluid in the chest was suspected. Repeated insertion of a needle, however, failed to reveal fluid. The sputum, however, changed in character, and examination now showed the presence of *S. haemolyticus* and *B. influenzae.* Finally, about two weeks after the second onset of fever, a small amount of dark, foul-smelling fluid was obtained by puncture, apparently from the lung. This showed the presence of *S. haemolyticus* and the staphylococcus. About a week later the chest was opened and a lung abscess was drained. Whether the occurrence of abscess was due to secondary infection with streptococci or whether this infection was secondary to the abscess formation is, of course, not certain.

There were two additional patients seen by us in the pneumonia ward who developed empyema, with *S. haemolyticus* in the fluid. One patient had never had measles and the other had had measles two weeks previously. In the case without measles, the occurrence of pneumonia was doubtful.

This patient had been slightly ill for two weeks previous to admission, but had been performing his duties. The pleural effusion was present on admission, so infection occurred outside the hospital. The sputum contained *S. haemolyticus* and *B. influenzae*, and the pleural fluid contained *S. haemolyticus*. The patient was operated on and recovered.

In the second case, which followed measles, there were signs of lobar pneumonia with empyema. The sputum contained only *S. haemolyticus* and *B. influenzae*. The pleural exudate contained *S. haemolyticus*. The patient was operated on, and his present condition is fairly favorable. It is possible that this patient had bronchopneumonia, and not lobar pneumonia.

These cases indicate the frequency of complicated pulmonary infections in the present epidemic, and they also show the difficulty of interpreting the course of events in certain cases. It is true that in most of these cases no careful observations were made during the early stages of the illness. It seems quite certain that lobar pneumonia may sometimes occur in patients already infected with streptococci and with bronchopneumonia already present in the lungs. That bronchopneumonia occurs secondarily to lobar pneumonia is not so well shown by our cases; but they do show that in cases of lobar pneumonia, secondary infection with streptococci not infrequently occurs. This is obviously of much practical importance, suggesting that, so far as possible, patients with lobar pneumonia should be protected from infection with this streptococcus.

PLACE AND MODE OF INFECTION IN POST-MEASLES BRONCHOPNEUMONIA

From the data previously presented, there appears little doubt that a hemolytic streptococcus is the chief, if not the only, cause of the bronchopneumonia following measles which occurs among the soldiers at this post.

We have previously indicated that the infection in these cases is probably descending, occurring first in

the throat, and successively involving the lower respiratory passages, and finally the lung. It therefore became of much interest and practical importance to learn whether hemolytic streptococci are present in the upper respiratory tract of all measles patients, and, if so, at what stage of the disease they are first present, or, on the other hand, whether these bacteria are present only in the throats of these patients who later develop pulmonary lesions.

We therefore first attempted to determine the prevalence of hemolytic streptococci in the throats of all the patients in the measles wards of this hospital. To do this, cultures were made from the pharynx and tonsils of these patients on blood-agar plates. The plates were incubated twenty-four hours and then studied for the presence of hemolyzing streptococci. These organisms were identified by isolation in pure culture from a single colony and by testing staining reaction, morphology, cultural characteristics, bile solubility, hemolytic activity and fermentation reactions. Hemolysis was determined by testing the power of a twenty-four hour broth culture to hemolyze an equal amount of a 5 per cent. suspension of the red blood cells of rabbits. The degree of hemolysis was recorded at the end of two hours at 37 C. Table 1 gives the results of the study.

TABLE 1.—INCIDENCE OF STREPTOCOCCUS HAEMOLYTICUS IN THROATS OF PATIENTS IN MEASLES WARDS

Total Number of Cases Examined	Number of Positive Cases	Number of Negative Cases	Per Cent. of Positive Cases
69	39	30	56.5

At the time of the examination, these patients had been in the measles wards for periods of time varying from one to fifty-five days. Of the sixty-nine patients examined, thirty-nine, or 56.5 per cent., showed the presence of *S. haemolyticus* in the throat.

These observations indicate that a large proportion of the patients confined to the measles wards harbor these organisms in the throat.

It next appeared of importance to learn whether or not this high incidence of carriers of hemolytic streptococci is peculiar to the measles wards or whether a similar state of affairs exists among the patients in other wards of the hospital. The incidence of strepto-

cocci of this variety in the throats of normal individuals under ordinary circumstances has not been determined accurately. In the presence of an epidemic of streptococcus infection, such as streptococcic sore throat, it has been found that a considerable number of healthy persons may carry this organism in the throat. On the other hand, the observers who have made fairly extensive studies on the flora of the normal throat, in the absence of epidemics of this kind, report that the occurrence of actively hemolytic streptococci in the throats is very rare. At the time of our arrival at San Antonio, it was evident that an epidemic of coryza, laryngitis and mild bronchitis existed among both the civil and military population. In some limited observations which we made, it was found that in the throats of persons suffering from this affection, hemolytic streptococci, and also influenza bacilli were occasionally present, singly or combined. It was possible, therefore, that the study of persons other than those suffering from measles might show a high incidence of hemolytic streptococci in the throats. Consequently cultures were made from the throats of patients in a ward in which the patients were suspected of having tuberculosis but who had no other disease. Table 2 presents the results of this study.

TABLE 2.—OCCURRENCE OF STREPTOCOCCUS HAEMOLYTICUS IN THE THROATS OF TUBERCULOSIS SUSPECTS (WARD 27)

Total Number of Cases Examined	Number of Positive Cases	Number of Negative Cases	Per Cent. of Positive Cases
28	6	22	21.4

The occurrence of *S. haemolyticus* in the throats of these patients is considerably less than the incidence among the measles patients. It should be mentioned that the patients in the tuberculosis ward are not rigidly isolated from patients in other parts of the hospital, transfers from this ward to another, and vice versa, not infrequently being made. Several cases of tonsillitis and pharyngitis were discovered during the process of making cultures. Moreover, these patients live in very close association, being confined in the ward and only a few of them being confined to bed.

There were two methods available to discover whether the measles patients acquired the hemolytic streptococci before admission, or whether transfer

from one patient to another probably occurred in the ward. One method was to make cultures on a large number of men in the barracks from which the patients with measles came, with the object of learning whether the incidence of streptococci in the throats of these healthy men was less than that among the men in the wards; the other was to make cultures from the patients with measles on admission to the hospital and then to repeat the examinations from time to time, in order to learn whether or not any of the patients with negative cultures later acquired the organisms. The latter method was chosen as consuming less time and more likely to give definite information. The results of the study are presented in Table 3.

TABLE 3.—OCCURRENCE OF STREPTOCOCCUS HAEMOLYTICUS IN THE THROATS OF MEASLES PATIENTS ON ADMISSION, AND THE SUBSEQUENT ACQUISITION OF THE ORGANISM IN THE CASES PREVIOUSLY NEGATIVE

		Per Cent.
Total number of cases examined	44	
Number of cases positive on admission	5	11.4
Number of cases positive 3 to 5 days after admission	17	38.6
Number of cases on final examination—8 to 16 days after admission	25	56.8

An analysis of this table indicates that a relatively small percentage of patients on admission to the measles wards harbor *S. haemolyticus* in their throats. However, as the time of residence in the ward increases, the number of carriers of *S. haemolyticus* increases, until finally the percentage of incidence becomes as high as that found in the measles wards in general. Because of these observations, there seems to be very little reason to doubt that a large percentage of measles patients acquire *S. haemolyticus* in their throats for the first time during their stay in the hospital wards.

While this study is not extensive enough to be absolutely conclusive, it indicates strongly that the high incidence of bronchopneumonia during convalescence from measles is directly related to the transfer of the infectious agent from one patient to another in the wards of the hospital.

These observations led us to suspect that the frequent occurrence of streptococcus complications, especially empyema, might also be related to the possible wide distribution of hemolytic streptococci among the

patients in the pneumonia wards. Although an effort has been made to admit to the wards assigned to the care of patients suffering from acute lobar pneumonia only patients suffering from this disease, it is quite certain that owing to the difficulties of diagnosis, a considerable number of patients with bronchopneumonia have been treated in these wards. We have already referred to certain of these cases.

To investigate this question, cultures were made from the throats of all the patients in two wards which contained only patients thought to have acute lobar pneumonia. Cultures were made from forty-five patients. The technic employed was exactly that used in the tests previously mentioned. It was found that twenty-six, or 57.7 per cent., of all these patients harbored hemolytic streptococci. In view of the high incidence of streptococcus infections among the lobar pneumonia patients, these results are most interesting and suggestive. There is no reason to believe that the percentage of patients carrying hemolytic streptococci on admission is larger than the percentage of measles patients who do so when admitted. This question, however, has not been investigated.

COMMENT AND CONCLUSIONS

The studies indicate that the cases of pneumonia at the base hospital, Fort Sam Houston, are chiefly of two varieties: first, acute lobar pneumonia, which does not differ essentially from that which occurs elsewhere; and second, bronchopneumonia, which in most cases, at present at least, follows measles.

The pulmonary lesions in most cases of this type of bronchopneumonia are characteristic and specific and have been studied and described by Dr. MacCallum. The etiologic agent in all the cases studied by us has been *S. haemolyticus*. There is no evidence presented by this work that indicates that pneumococcus causes the lesions and symptoms of this condition. Pneumonia following measles may be due to pneumococci, but the pulmonary lesion is then of the lobar variety. This complication of measles, however, is comparatively rare. Cases may occur in which both types of infection and both types of lesions are present. The sequence of events in such cases is difficult to determine and is probably not always the same.

Streptococcus infections following lobar pneumonia occur with considerable frequency in this hospital. Bronchopneumonia similar to that following measles may also probably occur as a sequel of acute lobar pneumonia, though the evidence for this is not conclusive. Whether in the cases of streptococcus empyema, complicating lobar pneumonia, pulmonary lesions due to the streptococci are always present or not, has not been determined.

The mortality in the cases of bronchopneumonia is very high; that of uncomplicated lobar pneumonia is low. Practically all the fatal cases of bronchopneumonia are complicated by empyema. The incidence of empyema among the uncomplicated cases of lobar pneumonia does not seem to be extremely high.

Our observations indicate that the number of measles patients harboring hemolytic streptococci on admission to the hospital is not large. The majority of the patients with measles acquire this organism during their stay in the hospital. The chance of developing postmeasles streptococcus infections is therefore increased by residence in this hospital.

A very large number of the patients suffering from acute lobar pneumonia have hemolytic streptococci in their throats. We have no direct evidence that they acquire these bacteria in the hospital, but the presumptive evidence indicates that many of them do so.

The work indicates that the high incidence of pneumonia in this hospital, and the resulting high mortality, has been due, to some extent at least, to infection occurring within the hospital itself. The conditions are not unlike those surrounding puerperal fever and surgical wound infections. While in measles, raw surfaces do not exist on which infection can occur, this disease renders the respiratory mucous membrane especially vulnerable to infection with streptococci. Possibly in other diseases, as scarlet fever and even lobar pneumonia, similar conditions exist. When infection is once started in a ward in which the patients are closely associated, the streptococci become widely distributed; they probably gain in virulence with repeated transfer through the human subject, and serious and widespread infection results.

Probably the conditions in this hospital are not unique. It is possible that the widespread incidence of fatal pneumonia in the other army hospitals may have a similar explanation.

PART II. PATHOLOGY[2]

By W. G. MacCallum, M.D.

The material for the following study was derived from thirty-seven necropsies performed on the bodies of patients who died in the base hospital of Fort Sam Houston, Texas. They were selected as cases of pneumonia, but in three of them it proved that death had resulted from other causes. Nevertheless, the lungs in these patients, as well as those from several other miscellaneous cases in which the necropsies were performed by the resident staff, were studied.

The results are by no means easy to analyze, since there are many complications, many combinations of different infections, and many variations arising from differences in the stages of the disease at which the patient died. Briefly stated, however, it appears that two main types of bacterial infection are concerned. On the one hand, there are cases due to infection with one or another form of the pneumococcus; on the other hand, many cases have occurred in which a hemolytic streptococcus is the etiologic agent. Other bacteria have been found, notably the influenza bacillus, a gram-negative bacillus of undetermined nature, and occasionally one or another of the staphylococci; but all of these appear to be rather accidental invaders, and it seems scarcely probable that they are in any way responsible for the main anatomic changes.

Analysis of the cases appears to show fairly conclusively that the pneumococcus is responsible for those in which lobar pneumonia was found. The *Streptococcus haemolyticus,* in most instances, seems to cause a peculiar form of bronchopneumonia, which on account of its anatomic characters I have designated "interstitial bronchopneumonia." There are, however, some cases in which this organism, growing in overwhelming numbers or with especial virulence, produces a patchy pneumonia of a type more closely resembling the familiar lobular or bronchopneumonia found so often as a terminal event in persons dying of some chronic disease, or in those in whom aspiration of infected material has occurred. This may be referred to as "lobular pneumonia."

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2. This part of the work was carried out with the assistance of Lieut. W. C. Von Glahn, M. R. C., U. S. Army.

One of these infections may be superimposed on the other, and there may even be found lesions corresponding to each in the same lung.

Fibrinopurulent pleurisy with abundant exudate has occurred with extreme frequency in these cases.

Since it is recognized that pneumonia frequently follows measles, this relation was especially studied. There were fifteen definite cases of measles in the series, and in eleven of these the interstitial bronchopneumonia was found. Two showed, at necropsy, lobar pneumonia alone, two lobular pneumonia alone, while two presented a combination of lobar and interstitial bronchopneumonia. In all there were seventeen cases of interstitial bronchopneumonia, and in the six cases of this condition not definitely following measles, no history of measles was obtained in five, although it was conceded that in the course of the great local epidemic these men might have passed through mild attacks of measles which were not mentioned when the clinical history was taken. The sixth case was at first regarded as measles, but later as scarlet fever. From all the cases of interstitial bronchopneumonia the hemolytic streptococcus was isolated, and it seems clear that this is the true causative factor, whether it gains entrance on the basis of a predisposing measles or otherwise. Details concerning all these relations will be given in full in a later report, but in this preliminary report it is necessary to describe the following conditions as they occurred in this series: (1) interstitial bronchopneumonia; (2) lobular pneumonia; (3) lobar pneumonia; (4) empyema; (5) combined infections; (6) other complications.

1. INTERSTITIAL BRONCHOPNEUMONIA

This is the condition already fairly well known through the work of Bartels, Delafield, Steinhaus, Hecht and others as occurring in children as a sequel of measles, whooping cough, etc. Their descriptions correspond closely with what we have found in adults, except in the general lack of complicating empyema in children, and in certain minor histologic details, notably the presence in the lungs of children of extraordinary giant cells derived from the epithelium. None of these writers determined the nature of the bacteria concerned. On the other hand, although it

has been recognized by various workers in this country that the hemolytic streptococcus is to be found in the bronchopneumonia following measles, none of them seems to have determined the exact nature of this peculiar bronchopneumonia. The association of the hemolytic streptococcus with the interstitial bronchopneumonia must, therefore, be especially emphasized.

The term "interstitial bronchopneumonia" was chosen as expressing briefly the salient features of the lesion. It may not be the most satisfactory term possible, because it fails to describe accurately the earliest stages, and leaves out of account the process of organization of the exudate which is very common; but any term that could describe the whole course of a progressive process would be unwieldy.

The interstitial bronchopneumonia has been studied in various stages in different cases and found to produce extraordinarily different appearances as it progresses.

In the earliest stage, the pleural surface of the lung is smooth and glistening. The lung is, in general, air containing, although atelectatic patches may be making their appearance. On section, small hemorrhagic foci are found scattered through the lung, each showing, as a rule, a gray rather opaque center. These foci measure from 2 to 3 mm. in diameter, sometimes more, and are so small that several may occur in one of the secondary lobules of the lung, that is, in one of the lobules marked off by the interlobular septa (W. S. Miller). Microscopically, it is found that these foci represent the ends of the bronchioles together with the adjacent alveoli. The bronchiole and the ductulus alveolaris are filled with leukocytes, among which streptococci are found in pairs or in short chains. There is some infiltration of the bronchial wall with leukocytes, and the adjacent alveoli contain a few leukocytes, occasional streptococci, coagulable fluid, and great numbers of red blood corpuscles. Not only the alveoli which form a continuation of the bronchiole, but also those which lie near its wall, seem to be affected.

In a somewhat later stage the lung can still be distended with air, although the patches of collapse are more extensive. On section it is found to be studded throughout large areas with small, gray nodules which project above the cut surface like miliary tubercles,

and are often surrounded by a red or grayish halo. At this time there may be visible a minute cavity or depression in the center of each which marks the lumen of the bronchiole. This may be represented, however, by the opaque contents of the bronchiole. These nodules have been mistaken by more than one for miliary tubercles, and it seems conceivable that the peculiar appearance of this and later stages may be in part, at least, responsible for the almost universal statement that measles is commonly followed by tuberculosis. Microscopically, such nodules are found to consist of a bronchiole filled with exudate of leukocytes, sometimes, but not often, associated with fibrin. The epithelial cell layer lining the bronchus is partly disintegrated or detached. The bronchial wall is hyperemic and thickened largely by the infiltration into its crevices of numbers of mononuclear wandering cells which have replaced the leukocytes. The alveoli about the bronchiole appear to contain less blood at this stage; only those immediately continuous with the ductulus alveolaris contain polymorphonuclear leukocytes; the others about the bronchiole usually contain a network of fibrin with mononuclear cells. The alveolar walls in the immediate neighborhood of the bronchiole are thickened by an infiltration of mononuclear cells (lymphocytes, plasma cells and larger wandering cells). Surprisingly few streptococci are found, and those chiefly in the bronchial exudate. Fibrinopurulent pleurisy, often with excessive effusion of greenish, turbid fluid, accompanies the process from this stage on.

In a still later stage the lung is usually much collapsed, dark blue, flabby, and airless except in the anterior portions. This is produced chiefly by the pressure of the pleural exudate, but partly by the occlusion of the bronchioles. At this stage, shotlike nodules 3 or 4 mm. in diameter may be felt all through the lung. On section, the pasty, airless lung sinks into a concave surface, leaving the gray peribronchial nodules projecting conspicuously. The interlobular septa have by this time become greatly thickened and infiltrated with cells and fibrin so that they stand out most conspicuously as whitish-yellow lines, marking out the whole lobulation of the lung in polygonal fields. In each of these fields there may be three or four pro-

jecting nodules which now usually show distinctly a central bronchial lumen. The surrounding tissue may be fairly dense, so that the peribronchial thickening is marked out chiefly by its opaque whiteness. Hemorrhage may in some cases stain the outlying regions about the nodules. If the bronchi be opened with the scissors, they are found to be slightly dilated toward the periphery of the lung, where they become thick walled as they run into the terminal portion which forms the center of the nodule. The contents are thick and glutinous. Microscopically, such a lung shows a very great infiltration of the bronchial wall with masses of mononuclear cells. The epithelium usually still persists in places, although much of it is desquamated. The lumen is filled with exudate of leukocytes with rather few chains of streptococci. Sometimes all the lining of the bronchus has disappeared so that in cross section it appears like an abscess. The walls of the adjacent alveoli are greatly widened and stuffed with mononuclear cells, desquamated epithelium, fluid and rather dense plugs of fibrin. Further out the alveolar walls are still thickened and infiltrated, and the alveoli contain chiefly fluid and desquamated epithelium. At this stage, organization of the exudate in the bronchi and the alveoli is usual. Indeed, this organization occurs with surprising rapidity, so that it may be quite advanced in patients who have apparently been ill only about ten days or two weeks. In the bronchi the new connective tissue and blood vessels arising from several points in the wall pervade the exudate and form richly vascular columns of fibrous tissue which extend into the alveoli and branch into each one. The lymphatics in the walls of the bronchi and blood vessels and in the interlobular septa are distended with mononuclear cells and fibrin, and contain numerous bacteria. The bacteria apparently reach the pleural network in this way, and this seems to be the most plausible explanation of the infection of the pleura. The interlobular septa and perivascular tissues are densely infiltrated with wandering cells and become very conspicuous. The pleural surface is covered with a thick, shaggy layer of fibrin, and the pleura itself is greatly thickened by being converted into a vascular granulation tissue which is gradually replacing the fibrin.

Streptococci are present in great numbers on the surface of the fibrinous exudate, as well as in the purulent fluid in the cavity of the pleura. It is to be noted that they, unlike the pneumococcus, are not to be found scattered everywhere in the meshes of the fibrin. It seems possible that they may digest and destroy the fibrin, but at any rate they are found only on its free surface. They are not engulfed by phagocytes as freely as are the pneumococci, and they are found less frequently in the tissues themselves. Even when in an inflamed tissue, such as the lobulated, fat masses which project into the pleura from the outside of the pericardial sac, streptococci are found in a matted layer over the free surface, they can be traced down into the crevices between the lobes of fat only so far as these are freely open. If the surfaces adhere no bacteria are found in the obliterated depth of the crevice.

In still later stages, more extensive infiltration of the peribronchial tissue occurs, and solid yellowish patches from 1 to 2 cm. in diameter appear. The induration about these, with edema and hemorrhage, becomes confluent, so that quite large areas may appear consolidated. As to the nature of the healing process and recovery from this change, we have had no opportunity to learn anything.

In one case in which in some parts of the lung the lesions just described occurred in a moderate stage of advancement, other areas showed a great increase in the number of streptococci, with a wide dissemination into the tissue and a correspondingly intense inflammatory reaction. In other cases, much later, after a long course in which empyema of long standing has been drained by operation, the lung has been found to contain extensive abscesses, sometimes confluent into large, purulent areas. In such cases, and in these alone, one may expect to find secondary lesions in distant organs. It is rather remarkable that this particular hemolytic streptococcus seems to be an organism of rather slight virulence, with no tendency to spread through the body. Septicemia occurs only in the hours just before death, if at all, and in only one protracted case was there found an infarct-like lesion in the spleen. In all the others, the abdominal organs were normal.

2. LOBULAR PNEUMONIA

In these cases there was evidently an overwhelming infection with a virulent organism, or what amounts to the same thing; the patient offered no resistance to the invasion. The lungs present irregular, patchy, hemorrhagic areas of consolidation which are not especially peribronchial or limited in size. In them the streptococci are found in amazing numbers, often in long, tangled chains, scattered through the alveolar contents as well as in the exudate in the bronchi. In this respect the condition contrasts with that found in the interstitial bronchopneumonia. The exudate itself is chiefly composed of polymorphonuclear leukocytes, with some blood. There is nothing especially characteristic about this process, but it does occur after measles and is sometimes associated with the formation of areas of necrosis of the whole tissue which subsequently assume the appearance of abscesses. These are really not typical abscesses, but rather necrotic areas of consolidated lung tissue loaded with great numbers of bacteria. There were four of these cases.

3. LOBAR PNEUMONIA

Thirteen cases of lobar pneumonia occurred in this series and presented the well known anatomic picture which need not be described. In ten of them the pneumococcus was found, but in the remaining three it was missed, apparently because it was overgrown by the hemolytic streptococcus or by other organisms, since all of these were protracted cases with empyema, in which death occurred some days after operation and drainage of the open pleural cavity.

In four cases, pneumococcus Type IV was isolated. Two showed the presence of Type I and two Type II. In two the type remained undetermined.

It seems very probable that in all the cases the lobar form of pneumonia was caused by the pneumococcus. In those in which the pneumococcus was not obtained in culture, organisms morphologically like them and having the characteristic distribution of the pneumococcus are seen in the sections of the affected lung.

Secondary infection with the hemolytic streptococcus seems to have occurred in some cases, although it remains difficult to tell whether the streptococcus may not have preceded the pneumococcus. In two

cases in which the pneumococcus seemed to predominate at necropsy, it was thought probable that the streptococcus infection had been followed by that with the pneumococcus. On the other hand, four or five cases showed the streptococcus in great numbers at necropsy, while the pneumococcus was found only in such lesions as a vegetation on the heart valve or an abscess in the rectus muscle. In one case the pneumococcus was found only in the pleural fluid. In another it had been present in the blood before death. In such cases it seemed probable that the pneumococcus had been outgrown and replaced by the streptococcus.

Of the thirteen cases, five showed the pneumococcus alone. In none of these was there any empyema or excessive outpouring of fluid pleural exudate. But of the remaining eight cases in which there was also a streptococcus infection, there was empyema in all except one, in which both pleural cavities were obliterated by old adhesions.

Certain histologic features with regard to the distribution of pneumococci may be mentioned. While in the case of the interstitial bronchopneumonia the streptococci are in most cases present in relatively small numbers and then confined chiefly to the exudate in the lumen of the bronchus and the immediately adjacent alveoli, to the contents of the lymphatic and the surface of the pleural exudate, the pneumococci in lobar pneumonia are present in great numbers and are scattered diffusely through the whole lung and everywhere through the pleural exudate. It is true that there are some cases of intense infection in which the streptococci grow in immense numbers throughout the affected portions of the lung; but ordinarily they are not to be found, or only rarely seen in the fibrinous exudate of the outlying alveoli. In the lobar pneumonia the pneumococci are rather more abundant in the bronchioles and ductuli alveolares than in the more peripheral alveoli; but many are to be found intimately mingled with the network of fibrin in all the alveoli and in the pleural exudate. The activity of phagocytes appears to be far greater in the case of the pneumococcus, so that great numbers of them are found enclosed in the leukocytes, while most of the streptococci appear to lie free in the exudate.

The transportation of the organisms by way of the lymphatic channels, in the walls of the blood vessels, and interlobular septa and pleura is striking in the case of the pneumococci, as well as of the streptococci. It seems probable, although not proved, that it is in this way that the pleura becomes infected. Injections of the lymphatics from the pleural network gave beautiful preparations showing the connections of this network with the enormous, deep lymphatics which run toward the hilum of the lung, in the walls of the bronchi and blood vessels, and in the septa. These aided in the recognition of the relation of the bacteria to the lymph channels.

4. EMPYEMA

Empyema occurred in twenty-six of the thirty-seven cases of the series. In every case in which there was empyema, *S. haemolyticus* was demonstrated, and although empyema occurs in pure pneumococcus infections, only those cases in this series in which there was also a streptococcus infection developed actual empyema. The exudate appears quite early in the cases of interstitial bronchopneumonia, and is usually a thin, turbid, greenish fluid with floating shreds of fibrin and a relatively thin, fibrinous covering over the lung. Usually this fibrinous exudate cannot be readily peeled off, but is intimately adherent to the lung and partly organized. Very large amounts of fluid may accumulate — in one instance several liters. The effect is, of course, largely mechanical, causing the collapse of the lung, with corresponding cessation of its function; but it seems that the presence of such a huge culture of streptococci, which appear to grow in enormous numbers in a position in which they are removed from actual contact with the tissues, must be a serious menace to the patient. Further studies should be made with regard to the toxic properties of this fluid and to the presence of bactericidal substances there.

After operation, the pleural cavity tends to become infected with various organisms which confer an extremely foul odor on the exudate. Encapsulated pockets of purulent fluid are often found between the lobes, even though the main cavity may have been fairly well emptied.

5. COMBINED INFECTIONS

Mention has already been made of the fact that both the pneumococcus and the streptococcus may occur in the same individual, and clinical study may show definitely which of these infections appeared first and which was superimposed. It is difficult to arrive at any conclusion as to this from the anatomic conditions, for the ordinary criteria of the duration of an inflammatory process—organization of exudate, production of mononuclear infiltration and indurative new growth of tissue in the framework of the lung —appear so rapidly in the interstitial bronchopneumonia and are so delayed in lobar pneumonia that they help but little.

In three cases there has been found in the lungs a definite intermixture of the anatomic lesions of lobar pneumonia with those of interstitial bronchopneumonia. These conditions seem to tend to exclude each other to some degree, even when they occur side by side in the same lung; but in some places the characteristic lesions of interstitial bronchopneumonia are found embedded in the uniform consolidation of a lobar pneumonia, emerging clearly into view as one leaves the area of lobar consolidation and passes over into the rest of the lung. In two cases the pneumococcus was recovered from the area of lobar consolidation, the streptococcus from the uncomplicated foci of interstitial bronchopneumonia in the same lung. These organisms are, however, too much alike, morphologically, to allow one to recognize them with certainty, in stained sections, in association with their specific lesions, when they occur together.

6. OTHER COMPLICATIONS

Complications with regard to other organs are rare in the cases of infection with this hemolytic streptococcus. Pericarditis occurred a few times, but most of the cases of pericarditis were associated with pneumococcus infection. Otitis media is recorded in several cases. There were two cases of acute nephritis, probably not dependent on this infection, since the kidneys in all other cases were normal. On the whole, there seems to be a very striking absence of involvement of any organs other than the lungs.

The range of complications in the case of pneumococcus infection has been rather greater. There were four cases of pericarditis, one of peritonitis, one of symmetrical bilateral abscess of the rectus abdominis muscles, and one in which death occurred suddenly in convalescence, from embolic occlusion of the pulmonary arteries.

SUMMARY

In the Army camps represented in this hospital, measles has been prevalent. Pneumonia occurred frequently, but not always as a sequel to measles. The nature of measles is unknown, and we have had no opportunity to learn what anatomic changes measles alone can produce. But it does produce coryza, conjunctivitis and laryngitis, and these conditions appear to predispose to infection of the respiratory tract with bacteria. This predisposition is made evident by the great proportion of the cases of the series in which streptococcus infection followed measles; but it is evident that streptococcus infection may occur in a person who has not had measles, and it is quite probable that other diseases, such as scarlet fever, predispose to its entrance in the same way as measles. When *S. haemolyticus* gained a foothold, it usually caused in this series of cases the anatomic complex called here interstitial bronchopneumonia." This is the same whether it is preceded by measles or scarlet fever, or by no other disease, and its characters are due to the specific effects of the streptococcus. When lobar pneumonia followed measles, the pneumococcus was in this series accompanied by the streptococcus, and in some cases the lobar pneumonia was complicated, anatomically, by the corresponding bronchopneumonia.

Infection with the hemolytic streptococcus does not always cause an interstitial bronchopneumonia, but may produce a patchy lobular pneumonia.

One of the most interesting features of our study of the cases in this hospital is the recognition of the invariable connection of *S. haemolyticus* with that characteristic anatomic lesion which was well known, but to which we have for convenience given the name "interstitial bronchopneumonia." This lesion is easily recognized in all its stages by its gross appearance, since the prominent, gray, solid peribronchial nodules with surrounding edema, hemorrhage, organization and

induration bear no resemblance to areas of pneumonic consolidation, which are homogeneous, solid patches, on the cut surface of which a plug of exudate projects from each alveolus. The microscopic appearance, as described above, is equally specific and characteristic, and there is no possibility of confusion with lobar or lobular pneumonia.

Empyema is a practically constant accompaniment of this condition, and is of extremely serious import.

The organism does not seem to be very virulent, and there is little tendency for it to enter the blood stream or to produce complicating lesions in distant organs.

Lobar pneumonia due to the pneumococcus has been found in many cases, not especially related to the occurrence of measles, but often complicated by secondary or coincident infection with *S. haemolyticus*. Its characters are exactly as seen elsewhere.